## IN THE DRAWINGS

Please add new Fig. 8 as a new drawing sheet to the originally-filed three sheets of drawings. The BRIEF DESCRIPTION OF THE DRAWINGS section of the specification has been amended to describe new Fig. 8. No new matter has been added. No annotated or replacement sheets are attached since this is a new figure.

Attachments: New Sheet (1)

## REMARKS

The Office Action of November 22, 2005 has been reviewed and the Examiner's comments carefully considered. The present Amendment amends claims 1 and 14, and adds new claim 15, all in accordance with the originally-filed specification. No new matter has been added. Further, claims 2 and 3 have been cancelled by the foregoing amendment, and claims 5-12 have been withdrawn. Accordingly, claims 1, 4 and 13-15 are pending in this application, and claim 1 is in independent form.

In the parent case to the presently-pending application, a Figure 1 was discussed in the "Background of the Invention" section illustrating the cutting action of a blade or knife according to known processes. However, although the description of this figure was included in the presently-pending application (*See* paragraph [0008]), the figure was inadvertently left out. Accordingly, the figure matching the description in this paragraph has been reinserted as Fig. 8, and the specification appropriately modified to refer to the new figure number. No new matter has been added. Insertion of this Fig. 8 into the present application is respectfully requested.

Non-English Prior Art

In Paragraph 2 of the Action, the Examiner indicates that the previously-filed Information Disclosure Statement fails to comply with 37 C.F.R. § 1.98(a)(3) as not including a concise explanation of the relevance of certain non-English prior art. In order to ensure full compliance, following are brief statements of the relevance of each document.

German Patent No. DE 913 112 discloses an older type of a microtome in which the cutting blade is horizontal and the sample moves horizontally for cutting and advances upwardly in steps between the cuts. The blade is fastened between two parallel leaf

springs and driven by magnets for oscillating movement parallel to the cutting edge. The cutting edge of a steel blade is relatively rough when viewed under an electron microscope and relatively blunt. With the oscillating motion of the blade, therefore, a sawing action is achieved: the jags of the cutting edge act like saw teeth. This sawing action of the blade in a microtome is also described in GDR Patent No. DD 156 199 in which the blade is driven by an electroacoustical transducer at high frequency, and in the Belgian patent, BE 440 928, which uses an ultrasound emitter to oscillate the blade. Applicant respectfully requests that the Examiner take these documents into consideration and indicate their consideration in the next Office Action.

The Examiner's Objections and Rejections

Initially, the Examiner has objected to the Abstract as including legal phraseology. In particular, the Examiner objects to the use of the term "said" in the abstract of the disclosure. The abstract has been modified through the foregoing amendment and the term "said" removed where appropriate. Accordingly, withdrawal of this objection is respectfully requested.

Claims 1-4, 13 and 14 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Examiner believes that these claims contain subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In particular, with reference to the first paragraph of page 4 of the specification, the Examiner does not believe that any structural description or drawings show how the blade is relatively moved with respect to the probe in the second direction. In

addition, the Examiner believes that it may instead be the probe that moves in the second direction.

Next, claims 1-4, 13 and 14 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Again, the Examiner requires additional clarity regarding the movement of the blade in a second direction, since the Examiner does not believe that the blade is capable of such movement. In addition, the Examiner requires additional information regarding the movement of the blade in the second direction at a constant speed.

With respect to the prior art, claims 1, 4 and 14 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 3,440,913 to Persidsky et al. (hereinafter "the Persidsky patent"). Further, claims 1-4, 13 and 14 stand rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,551,326 to Goodman in view of the Persidsky patent. In view of the foregoing amendments and the following remarks, Applicant respectfully requests reconsideration of the above-discussed rejections.

The Cited Prior Art

In the present Office Action, the Examiner has cited the above-referenced Persidsky patent and the Goodman patent as a basis of rejection. The Persidsky patent is directed to a microtome device (as opposed to an ultramicrotome device). In particular, the microtome of the Persidsky patent discloses a reciprocating knife edge, which moves along an arcuate path at a high velocity. As the Persidsky patent is a microtome device, it is used in the field of microtomy for cutting thin sections of a thickness of 0.5 to 50 micrometers. The Examiner understands the Persidsky patent to illustrate a tool that includes a blade block 17

with lateral vibration along the cutting edge in a first direction, and this vibration occurs between two spaced arms 4.

The Goodman patent is directed to an adhesive-less microtome boat which may be used in a microtome or an ultramicrotome. While the Examiner admits that the blade of the microtome boat of the Goodman patent does not vibrate in the manner claimed in the present invention, the Examiner believes that in view of the combination of the Goodman patent and the Persidsky patent, such a vibration is well known. Further, the Examiner believes that, in view of the Goodman patent, it would be obvious to experiment with a variety of amplitudes to arrive at an acceptable amplitude, such as about 1 μm.

The Present Invention

As set forth in independent claim 1 of the present application, as amended, the present invention is directed to a process for cutting sections from a probe for microscopic analysis. This process is achieved by using an *ultramicrotome* device having a blade with a cutting edge, where the cutting edge, in a non-vibrating position, extends at least approximately in a first direction. The process includes the steps of: (1) vibrating the blade in the first direction with an amplitude below about 1 μm; (2) between successive cuts, effecting relative movement between the probe and the blade in a second direction in a stepwise manner, where the second direction is perpendicular to the first direction; and (3) during each cut, effecting relative movement between the probe and the blade in a third direction perpendicular to the first and second directions, whereby the probe is cut in sections having a thickness of about 10 nm to about 100 nm.

*Relative* Movement in the Second and Third Directions

With respect to the Examiner's Section 112 (first and second paragraphs) rejections of claims 1-4, 13 and 14, Applicant respectfully offers the following explanation and description. In Paragraph 4 of the Action, the Examiner indicates that it is the probe that moves in the second direction, as opposed to the blade. Applicant submits that the Examiner is correct that in the embodiment shown in the present application, the blade is, indeed, stationary in the second direction, while the probe moves in this direction instead. However, it is important to note that both the "old" and the "new" claim language in independent claim 1 refer to *relative* movement. Therefore, regardless of whether the probe or the blade moves in *absolute* terms, i.e., relative to a bench on which the ultramicrotome is placed, there is effected a *relative* movement between the blade and the probe. It is this *relative* movement that is achieved or effected in the second and third directions.

Independent claim 1 has been modified by the foregoing amendment. In particular, this claim now states that, "between successive cuts, relative movement is effected between the probe and the blade in a second direction in a stepwise manner...". In addition, during each cut, relative movement is effected between the probe and the blade in a third direction perpendicular to the first and second directions. Therefore, the claim language has been modified to better define and explain the movement, that is the relative movement, between the blade and the probe.

Still further, Applicant respectfully refers the Examiner to paragraph [0040] of the specification, where this "relative movement" is further discussed as follows:

> [0040] Of course, the relative movement between the knife 1 and the probe 3 can be achieved in different ways than the one specifically shown in Fig. 6., e.g., the slide 73 and/or the slide 77 could be associated with the holder 19 instead of with the chuck 80, or the horizontal and vertical

> vibrations could be reversed, i.e., that the knife 1 oscillates vertically and the chuck 80 horizontally, or both vibrations could be imparted on the same elements, knife 1 or chuck 80.

Accordingly, it is envisioned that the slide 73 and/or the slide 77, which serve to impart a movement on the probe in the second and third directions, can be associated with the holder 19 (i.e., the blade) instead of with the chuck 80 (i.e., the probe). Accordingly, with such an arrangement, it would be the blade that moves in the second and/or third direction, while the probe would remain stationary. However, and regardless of which arrangement, relative movement is effected between the probe and the blade. Therefore, independent claim 1, as amended, encompasses a situation where the probe "moves" *relative* to the blade, or where the blade moves in the second and/or third direction in absolute terms, while the probe is stationary in such direction.

In order to better understand the terms "second direction" and "third direction", independent claim 1 has also been amended to more clearly clarify that the second direction is the direction in which the thickness is adjusted, which means it is the direction in which the relative movement between the probe and the blade between cuts and in a stepwise manner. Further, the third direction is the cutting direction, which means it is the direction in which the relative movement between the probe and the blade is effected during each cut. A more detailed explanation can be found in paragraph [0033] of the originally-filed specification. Applicant believes that the amendments to independent claim 1, together with the accompanying description in the specification, more clearly explain the movements between the blade and the probe at the various points in the process.

Claim 14 has also been amended to better set forth the movement between the probe and the blade. Again, this movement is considered *relative* movement between the

probe and the blade, which may be effected at a substantially constant cutting speed. The Examiner's point regarding acceleration and deceleration is understood, and dependent claim 14 has been appropriately modified to more clearly set forth that this relative movement is at a constant speed only during each cut. The Examiner is correct that, between cuts, there will be an acceleration and deceleration in this direction, as well as some additional movement back into the starting position. Accordingly, the constant cutting speed is attained during each cut, as opposed to between cuts, as is now specifically set forth in claim 14.

Effective and Relative Movement Between the Blade and Probe in Three Distinct Directions

As discussed above, the present invention is a process for cutting sections from a probe for microscopic analysis that utilizes an *ultramicrotome* device having a blade with a cutting edge. The blade is vibrated in the first direction with an amplitude below about 1 μm, and in between successive cuts, relative movement is effected between the probe and the blade in a second direction in a stepwise manner. The second direction is perpendicular to the first direction. In addition, during each cut, relative movement is effected between the probe and the blade in a third direction perpendicular to the first and second directions. In this manner, the probe is cut in sections having thicknesses of about 10 nm to about 100 nm. Accordingly, the process of the present invention is clearly in the specialized field of ultramicrotomy.

Applicant submits that the Persidsky patent teaches a microtome device, as opposed to an ultramicrotome device. In fact, the Persidsky patent is entitled "Microtome". While the Examiner may believe that the differences in microtomy and ultramicrotomy are negligible, for one of ordinary skill in the art, there is a vast difference between an ultramicrotome device and a microtome device. In particular, microtomy is used for cutting

thin sections of a thickness of 0.5 to 50 micrometers. These thin sections or samples are used for analysis under an optical microscope. The problems that exist in microtomy are that the specimen to be cut is typically distorted, abraded or non-uniformly cut, if the blade is not applied in the right angle at the beginning of a cut. The cutting procedure, however, is not very problematic.

With respect to ultramicrotomy, much thinner sections need to be cut. These sections or samples are used in electron microscopes. For example, the thickness of the sample range utilized is between 10 nm and 100 nm, which represents a 5 to 50-times reduction with respect to the thickness used in microtomy. Performing cuts in an ultramicrotomy process is much more complicated than cuts performed in microtomy, since the surrounding materials change during the cut. Specifically, the material is compressed during the application of the knife or cutting implement, and this compression is quite small and can only be seen under the electron microscope, i.e., long after the specimen has been cut into sections.

In order to assist the Examiner in observing this phenomenon, attached to the present Amendment is a printout of an electron microscope showing a sample of a yeast cell being cut without vibrating the knife (and therefore being compressed) and a sample of a yeast cell being cut by a vibrating knife in a process according to the present invention (and, therefore, showing its real circular shape). The first sample is useless for analysis with an electron microscope, and the second sample is perfectly acceptable for such analysis. In microtomy, the samples are so thick that this compression does not occur. Still further, these compressions will not disturb the analysis under the optical microscope.

In addition, in ultramicrotomy, a problem exists known as "chatter". Chatter is caused by a rapid vibration of the knife blade, resulting either from an unsharpened blade or from external vibrations being transmitted to the blade. This phenomenon of "chatter" is well known in the field, and results in alternate thick and thin regions in the sections. Much effort has been spent in the field of ultramicrotomy to avoid chatter. In particular, much care has been taken in the art to avoid any vibrations of the ultramicrotome which might be transmitted to the blade and which might cause chatter. The problem of chatter thus has led to a prejudice in the field that any vibration of the blade must be strictly avoided. Accordingly, Applicant submits that a person of ordinary skill in the art would be familiar with this problem and would not consider the teachings of the Persidsky patent to be applicable in this technological field, since the vibration of the knife would be expected to lead to chatter, which is a problem that must be avoided. The present invention overcomes this prejudice. It is the merit of the present invention to have shown that, by applying controlled vibrations substantially parallel to the cutting edge with a small amplitude below about 1 micrometer, uncompressed slices can be obtained without the alternating thin and thick regions which are typical of chatter. Thus, the process of the present invention leads to slices which are neither distorted by compression nor by chatter. In the view of the prevailing prejudice in the field, this was completely unexpected. Applicant submits that, already for this reason, the skilled person would not combine the teachings of Goodman with those of Persidsky.

Still further, it appears that the Examiner believes that the microtome of the Persidsky patent can be used to cut any thicknesses by use of adjustable knob 43. In particular, the Examiner indicates that since knob 43 controls the thickness in an analog manner, it can be set at any setting, including between 10 nm and 100 nm, and therefore can

be used as an ultramicrotome. Applicant respectfully submits that the Persidsky patent is not capable of cutting slices at a thickness between 10 nm and 100 nm. The top of the knob 43 is provided with a thickness counter in microns (*see* col. 4, lines 36-38 and Fig. 1, "SECTION THICKNESS (MICRONS)"). Accordingly, this counter only provides for readings in steps of whole microns. A setting below one micron appears to be impossible, let alone a setting in the claimed region of 10 nm and 100 nm. Applicant therefore submits that a skilled artisan in the field of ultramicrotomy would never consider using the microtome device of the Persidsky reference, especially in view of the inability of the microtome of the Persidsky patent to effectively cut samples to the required and extremely fine thickness.

Still further, even if the skilled artisan in the field of ultramicrotomy would, for some reason, refer to a 1969 patent on a microtome, he would necessarily arrive at a process in which the amplitude of the vibration would be way too large. It is readily apparent from the setup and arrangement of the microtome of the Persidsky patent, which includes an electromagnetic driving microphone, that the amplitude of vibration would exceed one micron by at least one or two orders of magnitude. With respect to the present invention, in order for the claimed process to work properly, the amplitude is important, and a vibration in the range implicit from the Persidsky patent would not lead to any satisfactory results.

Still further, it appears that the Examiner may believe that it is in the realm of ordinary and routine experimentation to arrive at an amplitude below one micron. However, Applicant respectfully submits that the arrangement and microtome of the Persidsky patent would not allow such a low amplitude setting. Further, the skilled artisan in the field of ultramicrotomy who is confronted with a device performing a movement in the range of

hundreds or thousands of microns, would simply not consider reducing amplitude to a range below one micron.

With respect to the Goodman patent, this reference is directed to an adhesive-less microtome boat for use in connection with a microtome device. The Examiner admits that the blade of the device of the Goodman patent does not vibrate as set forth in the claims of the present application. Instead, the Examiner relies on the Persidsky patent for such vibration. Applicant has already distinguished the present invention and claims the present application from the microtome of the Persidsky patent, such that the combination of the Goodman patent and the Persidsky patent does not cure these deficiencies.

In addition, Applicant submits that the Goodman patent actually is much more supportive of Applicant's argument regarding the clear differences between microtomy and ultramicrotomy. For example, the Examiner refers to column 1, line 31 of the Goodman patent for teaching the cutting of thicknesses between 10 nm and 100 nm. Applicant submits that all of the citations of the Examiner to the Goodman patent are to the "Background Art" section of this reference, which clearly differentiates between an "ultramicrotome" and a "microtome". While the "adhesive-less microtome" of the Goodman patent may be used in connection with either a microtome or an ultramicrotome knife, this only provides further basis for understanding the differences between the devices and the applicable and technological fields of microtomy and ultramicrotomy.

Summary

The present invention is a process for cutting sections from a probe for microscopic analysis using an *ultramicrotome* device. The blade of the device vibrates in a first direction with an amplitude *below about 1 μm*. Between successive cuts, relative

movement is effected between the probe and the blade in a second direction, and during each cut, relative movement is effected between the probe and the blade in a third direction. In addition, the second direction is perpendicular to the first direction, and the third direction is perpendicular to the first and second directions. In this manner, the probe is cut into sections having a thickness of *about 10 nm to about 100 nm.* Importantly, by using this specific orientation of directions and vibration, "chatter" is drastically reduced, and compression is avoided. Therefore, the process of the present invention is more efficient and effective in providing cut sections having a thickness of about 10 nm to about 100 nm in the field of ultramicrotomy.

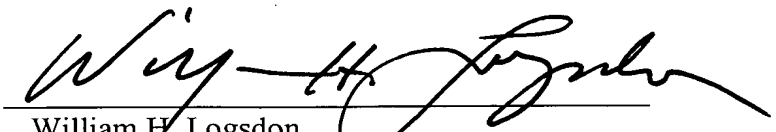
For the foregoing reasons, Applicant submits that none of the Persidsky patent, the Goodman patent nor any of the cited prior art, whether used alone or in combination, teach or suggest a process for cutting sections from a probe as specifically set forth in independent claim 1 of the present application, as amended. Accordingly, independent claim 1 is not anticipated by or rendered obvious over the cited prior art. There is no hint or suggestion in any of the references cited by the Examiner to combine these references in a manner which would render the invention, as claimed, obvious. Accordingly, reconsideration of the rejection of independent claim 1 is respectfully requested.

Claims 4 and 13-15 depend directly from and add further limitations to independent claim 1 and are believed to be allowable for the reasons discussed hereinabove in connection with independent claim 1. Further, specifically with respect to new dependent claim 15, Applicant notes that the Persidsky patent discloses frequencies in the range of 45 to 137 cycles per second (*see* col. 2, lines 62-63 of the Persidsky patent). Again, this is at least two orders of magnitude distant from the instantly-claimed frequency range. The microtome

of the Persidsky patent would obviously not be capable of oscillations in the ultrasound range, and the skilled artisan would definitely not consider vibrating the blade in the ultrasound range when considering the teachings of the Persidsky patent. Therefore, for all the above reasons, reconsideration of the rejections and allowance of claims 4 and 13-15 are respectfully requested.

For all the foregoing reasons, Applicant believes that claims 1, 4 and 13-15, as amended and added, are patentable over the cited prior art and in condition for allowance. Reconsideration of the rejections and allowance of all pending claims 1, 4 and 13-15 are respectfully requested. If the Examiner wishes any further clarifications in the differences between an ultramicrotome and a microtome, ultramicrotomy and microtomy, or the devices of the prior art and the process of the present invention, he is encouraged to please contact the undersigned at his convenience. In addition, if the Examiner desires a Declaration from one skilled in the art setting forth these differences, the undersigned asks the Examiner to please advise.

Respectfully resubmitted,
THE WEBB LAW FIRM

By 

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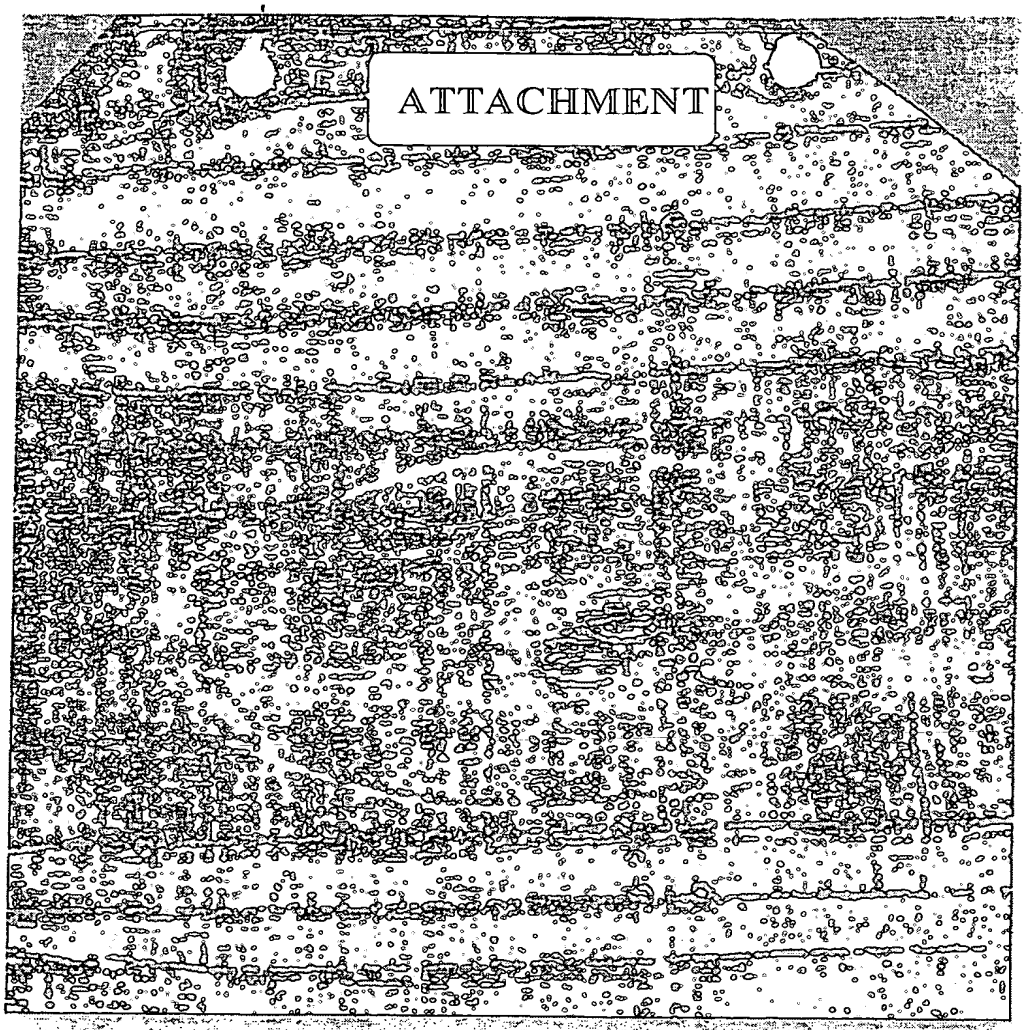
ATTACHMENT



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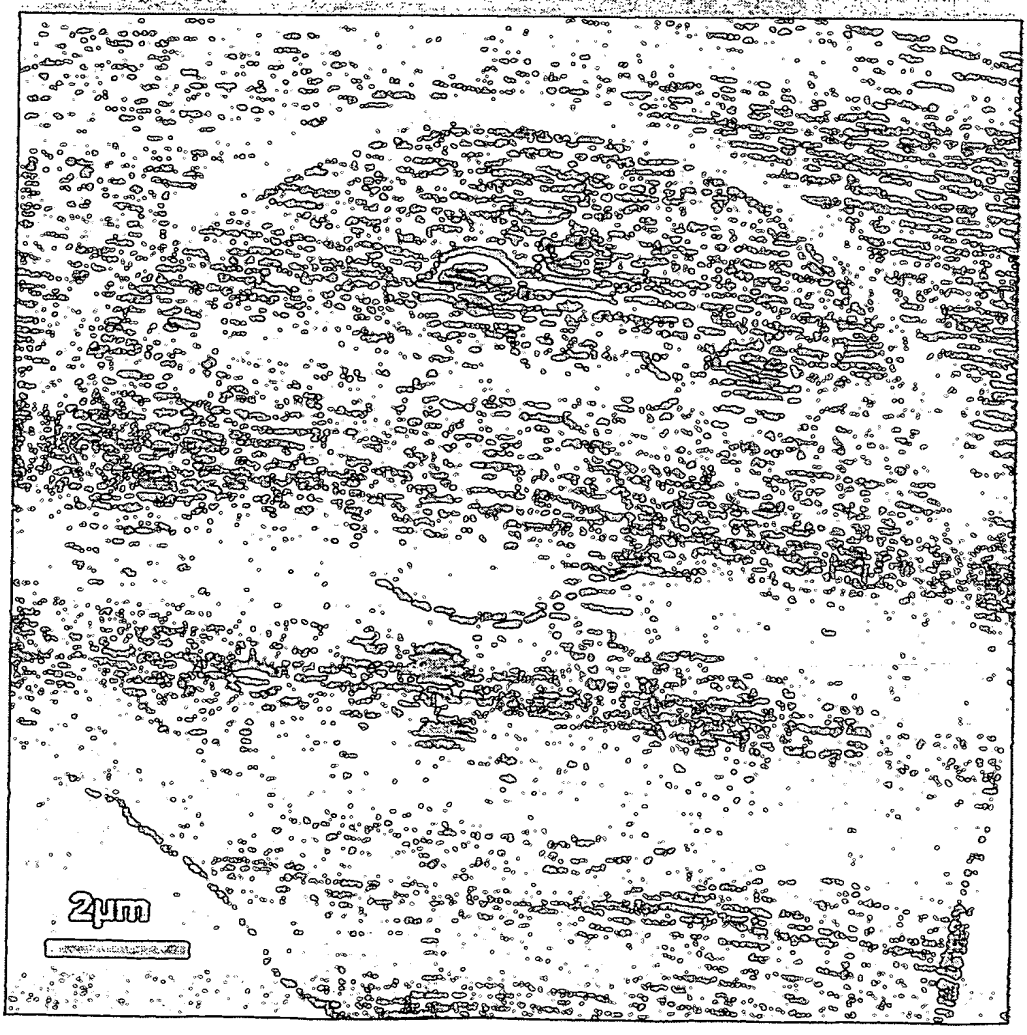


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